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10/568,507	02/16/2006	Nobuko Yamamoto	03500.103811.	1163

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EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,507	YAMAMOTO, NOBUKO	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-11 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-11 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/1/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 June 2009 has been entered.

Status of the Claims

2. This action is in response to papers filed 22 June 2009 in which claims 1 and 9-11 were amended, claims 4-8 and 12-21 were canceled, and new claims 22-25 were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1, 9-11, and 22-25 are under prosecution.

Information Disclosure Statement

3. The Information Disclosure Statement filed 1 July 2009 is acknowledged and has been considered.

4. The following rejections are new rejections necessitated by the amendments.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22 and 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 22 and 24 are indefinite in claim 22, which recites the limitation "based on expected amounts of the target substances in the solution" at the end of the claim. The recitation is indefinite because the number of probe spots depends upon expected amounts in a solution, which not part of the claimed carrier, and which is dependent the target solution used and can vary between different target solutions. For example, a carrier having a first area has ten spots to a first gene and a second area having twenty spots to a second gene. A target solution has twice as much expression of the second gene as the first, and the carrier infringes upon the claim. A second target solution has equal amounts of expression in both genes. Thus, the same carrier that infringes upon the claim if used with the first target solution does not infringe upon the claim if used with the second target solution. The metes and bounds of the claims are thus unclear because the same carrier infringes claim 22 if it is used with the first target solution but does not infringe claim 22 if it is used with the second target solution. Therefore, infringement could not be assessed and the claim is indefinite.

B. Claim 24 is indefinite because the term "practically" in claim 24 is a relative term which renders the claim indefinite. The term "practically" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus, the recitation "practically equal" is indefinite because the metes and bound of "practically" (e.g., +/- 10%, 15% etc) are not defined either by the claim or the specification.

C. Claim 25 is indefinite in the limitation "wherein the number of spots in each of the areas is proportional to an average amount of expression, in a human, of a target gene having a sequence complementary to a respective one of the probes" at the end of the claim. The recitation is indefinite because the number of probe molecules depends on the amount of target in a human, wherein the amount of target is "a human" is dependent upon which human is used and can vary between different human subjects. For example, a carrier having a first area has ten spots to a first gene and a second area having twenty spots to a second gene. A first human subject has twice as much expression of the second gene as the first, and the carrier infringes upon the claim. A second human subject has equal amounts of expression in both genes. Thus, the same carrier that infringes upon the claim if used with the first human patient does not infringe upon the claim if used with the second human patient. The metes and bounds of the claims are thus unclear because the same carrier infringes claim 24 if it is used with the first human but does not infringe claim 24 if it is used with the second human. Therefore, infringement could not be assessed and the claim is indefinite.

Claim Rejections-35 USC § 102(a, b, e)

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002).

Regarding claim 1, Alfenito teaches a probe carrier in the form of a nylon membrane, which is a carrier, having spots of oligonucleotides (i.e., probes) on the surface (Example 8). The array comprises two or more areas containing respective one of the probes as separated spots on the probe carrier; namely, the arrays on the carrier comprise separate subarrays of spots, which are known locations, wherein separate subsets of arrays are formed by avoiding spotting is some of the rows and or columns of the array (Example 8), thus creating spot subarrays each having different numbers of spots. Each subarray is to a different person having different polymorphisms (i.e., gene

alleles; Example 24); thus, each subarray has a different number of spots and depending on the different alleles therein.

Regarding claim 10, Alfenito teaches the carrier of claim 1.

It is noted that the courts have stated:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP§ 2113.

The limitation regarding the use of ink jet methods are part of the process of making the carrier rather than structural limitations of the carrier. Because the Alfenito teaches the structural elements of claim 1, claim 10 is also anticipated by Alfenito.

9. Claims 1, 9-10, and 22-24 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004, filed 25 November 2003).

It is noted that the previous Office Action incorrectly stated that Kronick et al is a 102(b) reference. The examiner regrets any confusion caused by this error.

Regarding claim 1, Kronick et al teach a probe carrier comprising a carrier in the form of a solid support (Abstract and Figure 6) having thereon a plurality of probe spots (i.e., features; paragraph 0063). The array comprises different regions, wherein each region comprises multiple features (paragraph 0014), and each feature is a spot

(paragraph 0030). The address of each spot, feature, and region is known because the array is fabricated (paragraph 0030). Kronick et al teach different probes that capable of specifically binding to a target substance (paragraph 0090), and the probes bind to genes (paragraph 0166). Kronick et al also teach the relative total feature areas (i.e., regions) have different numbers of features of the same size and that the population or probes therein are dependent upon the suspected relative abundance of the targets (paragraph 0090); thus, the carrier comprises two different areas (regions) comprising features (spots) to different genes, and the number of spots in each region is different because the number of spots depends on the expected abundance of the target detected in each area.

Regarding claim 9, Kronick et al teach the carrier of claim 1, wherein the amount of probe molecules per spot is the same for the same probe and different between probes having different sequences; namely, features within a region have the same probe density and the different regions have different probe densities (paragraph 0014).

Regarding claim 10, the carrier of claim 1 is discussed above.

As noted above, the courts have stated that if the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. The limitation regarding the use of ink jet methods are part of the process of making the carrier rather than structural limitations of the carrier. Because the prior art teaches the structural elements of claim 1, claim 10 is also anticipated by Kronick et al.

Regarding claim 22, Kronick et al teach the carrier of probe 1, wherein the number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio; namely, the number of probes is proportional to the square root of the expected signal for each target (paragraph 0097).

Regarding claim 23, Kronick et al teach the method of claim 1, wherein the amount of probes immobilized per spot is known; namely, $6x10^{10}$ probes per spot (i.e., feature) is immobilized (paragraph 0097).

Regarding claim 24, Kronick et al teach the method of claim 1, wherein the amount of probe molecules per spot is practically equal among all probes; namely, the different regions have the same feature probe density (i.e., numbers of probes per feature; paragraph 0063), but different numbers of features of the same size (paragraph 0090).

Claim Rejections - 35 USC § 102(a,e)/103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1, 10, and 23 are rejected under 35 U.S.C. 102(a,e) as anticipated by Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003) in view of Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002).

Regarding claim 1, Ares et al teach a probe carrier in the form of a substrate, which is a carrier, having spots of oligonucleotides (i.e., probes) on the surface (paragraph 0071). The array comprises two or more areas containing respective one of the probes as separated spots on the probe carrier; namely, the carrier comprises a plurality of different oligonucleotide spot patterns, wherein each spot pattern is to a different target nucleic acid (paragraph 0072). Each different target nucleic acid is a different gene (paragraph 0074), thus, each different pattern of spots is to a different gene. The spot locations are known because the pattern is known (paragraph 0065). Ares et al also teach the carrier is used for quantification of the two or more genes; namely, the probes allow for quantified measure of the concentration of the hybridized (i.e., target) nucleic acid (paragraph 0125).

The preceding rejection is based on judicial precedent following *In re Fitzgerald*, 205 USPQ 594, because Ares et al are silent with regard to the number of spots in each pattern being different. However, the different number of spots depending on the gene recited in claim 1 is deemed to be inherent in the Ares et al because Ares et al teach the patterns are different (paragraph 0072) and the patterns include an organized grid of

rows and columns, or a circle, or other shapes (paragraph 0065). A circular pattern would have a different number of spots than a grid. The burden is on Applicant to show that the claimed different number of spots is either different or non-obvious over that of Ares et al.

Alternatively, Alfenito teaches carriers in the form of DNA arrays which comprise separate subarrays of spots, wherein separate subsets of arrays are formed by avoiding spotting is some of the rows and or columns of the array (Example 8), thus creating spot subarrays each having different numbers of spots. Alfenito also teaches the use of the different subarrays has the added advantage of allowing parallel analysis of many sample types (column 10, lines 10-20). Thus, Alfenito teaches the known technique of using different numbers of spots in different arrays.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier comprising different arrays having different patterns of spots as taught by Ares et al so that the different patterns of spots have different numbers of spots as taught by Alfenito to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing parallel analysis of many sample types as explicitly taught by Alfenito (column 10, lines 10-20). In addition, it would have been obvious to the ordinary artisan that the known technique of using the known technique of using different numbers of spots in different arrays of Alfenito could have been applied to the carrier of Ares et al with predictable results because the

known technique of using the known technique of using different numbers of spots in different arrays of Alfenito predictably results in a reliable carrier having different subarrays.

Regarding claim 10, the carrier of claim 1 is discussed above. Ares et al teach the spots are formed by an ink jet method (paragraph 0082).

In addition, as noted above, the courts have stated that if the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. The limitation regarding the use of ink jet methods are part of the process of making the carrier rather than structural limitations of the carrier. Because the prior art teaches the structural elements of claim 1, claim 10 is also anticipated by Ares et al, or, alternatively, obvious over Ares et al in view of Alfenito.

Regarding claim 23, the carrier of probe 1 is discussed above. Ares et al also teach the amount of probes per immobilized spot is known; namely, 1 ng of probes are present in the spots (paragraph 0075).

Claim Rejections - 35 USC § 103

12. Claims 1, 9, 22, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002) in view of Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiments of dependent claims 9, 22, and 24.

Regarding claim 9, Alfenito teaches the probe carrier of claim 1 in the form of a nylon membrane, which is a carrier, having spots of oligonucleotides (i.e., probes) on the surface (Example 8). The array comprises two or more areas containing respective one of the probes as separated spots on the probe carrier; namely, the arrays on the carrier comprise separate subarrays of spots, which are known locations, wherein separate subsets of arrays are formed by avoiding spotting is some of the rows and or columns of the array (Example 8), thus creating spot subarrays each having different numbers of spots. Each subarray is to a different person having different polymorphisms (i.e., gene alleles; Example 24); thus, each subarray has a different number of spots and depending on the different alleles therein.

Alfenito does not teach the amount of probe molecules per spot is the same for the same probe and different between different probe sequences.

However, Kronick et al teach a carrier wherein the amount of probe molecules per spot is the same for the same probe and different between probes having different sequences; namely, features within a region have the same probe density and the different regions have different probe densities (paragraph 0014). Kronick et al also teach the probe densities have the added advantage of allowing customized arrays to be made for a target (paragraph 0076). Thus, Kronick et al teach the known technique of providing amounts of probe molecules per spot that are the same for the same probe bur are different between different probe sequences.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier as taught by Alfenito so that the amount of probe molecules per spot is the same for the same probe and different between different probe sequences as taught by Kronick et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing customized arrays to be made for a target as explicitly taught by Kronick et al (paragraph 0076). In addition, it would have been obvious to the ordinary artisan that the known technique of having the amount of probe molecules per spot the same for the same probe and different between different probe sequences as taught by Kronick et al could have been applied to the carrier of Alfenito with predictable results because the known technique of having the amount of probe molecules per spot the same for the same probe and different between different probe sequences as taught by Kronick et al predictably results in an array configuration useful in detecting genes.

Regarding claims 22 and 24, the carrier of probe 1 is discussed above.

Alfenito does not teach the number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio (i.e., claim 22) or the amount of probe molecules per spot is practically equal among all probes (i.e., claim 24).

However, Kronick et al teach a carrier wherein the number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is

expected to be at a lower ratio; namely, the number of probes is proportional to the square root of the expected signal for each target (paragraph 0097). Kronick et al also teach the amount of probe molecules per spot is practically equal among all probes; namely, the different regions have the same feature probe density (i.e., numbers of probes per feature; paragraph 0063), but different numbers of features of the same size (paragraph 0090). Kronick et al also teach the probe densities have the added advantage of allowing customized arrays to be made for a target (paragraph 0076). Thus, Kronick et al teach the known technique of providing amounts of probe molecules so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio (i.e., claim 22) and that the amount of probe molecules per spot is practically equal among all probes (i.e., claim 24).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier as taught by Alfenito so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio (i.e., claim 22) and that the amount of probe molecules per spot is practically equal among all probes (i.e., claim 24) as taught by Kronick et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing customized arrays to be made for a target as explicitly taught by Kronick et al (paragraph 0076). In addition, it would have been obvious to the

ordinary artisan that the known technique of providing amounts of probe molecules so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio and that the amount of probe molecules per spot is practically equal among all probes as taught by Kronick et al could have been applied to the carrier of Alfenito with predictable results because the known technique of providing amounts of probe molecules so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio and that the amount of probe molecules per spot is practically equal among all probes as taught by Kronick et al predictably results in an array configuration useful in detecting genes.

13. Claims 9, 22, and 24 are rejected under 35 U.S.C. 103(a) as obvious over Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003) alternatively in view of Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002) as applied to claim 1 above, and further in view of Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004).

Regarding claim 9, the carrier of claim 1 is discussed above in Section 11.

While Ares et al teach the spots correspond to human genes (paragraph 0072), neither Ares et al nor Alfenito teach the number of probe molecules is different for the different sequences.

However, Kronick et al teach a carrier wherein the amount of probe molecules per spot is the same for the same probe and different between probes having different sequences; namely, features within a region have the same probe density and the different regions have different probe densities (paragraph 0014). Kronick et al also teach the probe densities have the added advantage of allowing customized arrays to be made for a target (paragraph 0076). Thus, Kronick et al teach the known technique of providing amounts of probe molecules per spot that are the same for the same probe bur are different between different probe sequences.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier as taught by Ares et al (alternatively in view of Alfenito) so that the amount of probe molecules per spot is the same for the same probe and different between different probe sequences as taught by Kronick et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing customized arrays to be made for a target as explicitly taught by Kronick et al (paragraph 0076). In addition, it would have been obvious to the ordinary artisan that the known technique of having the amount of probe molecules per spot the same for the same probe and different between different probe sequences as taught by Kronick et al could have been applied to the carrier of Ares et al (alternatively in view of Alfenito) with predictable results because the known technique of having the amount of probe molecules per spot the same for the same probe and different between different probe

sequences as taught by Kronick et al predictably results in an array configuration useful in detecting genes.

Regarding claims 22 and 24, the carrier of probe 1 is discussed above.

Neither Ares et al nor Alfenito teach the number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio (i.e., claim 22) or the amount of probe molecules per spot is practically equal among all probes (i.e., claim 24).

However, Kronick et al teach a carrier wherein the number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio; namely, the number of probes is proportional to the square root of the expected signal for each target (paragraph 0097). Kronick et al also teach the amount of probe molecules per spot is practically equal among all probes; namely, the different regions have the same feature probe density (i.e., numbers of probes per feature; paragraph 0063), but different numbers of features of the same size (paragraph 0090). Kronick et al also teach the probe densities have the added advantage of allowing customized arrays to be made for a target (paragraph 0076). Thus, Kronick et al teach the known technique of providing amounts of probe molecules so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio (i.e., claim 22) and that the amount of probe molecules per spot is practically equal among all probes (i.e., claim 24).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier as taught by Ares et al (alternatively in view of Alfenito) so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio (i.e., claim 22) and that the amount of probe molecules per spot is practically equal among all probes (i.e., claim 24) as taught by Kronick et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing customized arrays to be made for a target as explicitly taught by Kronick et al (paragraph 0076). In addition, it would have been obvious to the ordinary artisan that the known technique of providing amounts of probe molecules so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio and that the amount of probe molecules per spot is practically equal among all probes as taught by Kronick et al could have been applied to the carrier of Ares et al (alternatively in view of Alfenito) with predictable results because the known technique of providing amounts of probe molecules so that number of spots is higher for a target that is expected to be at a higher ratio than the number of spots for a target that is expected to be at a lower ratio and that the amount of probe molecules per spot is practically equal among all probes as taught by Kronick et al predictably results in an array configuration useful in detecting genes.

14. Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002) in view of Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiment of dependent claim 11.

Regarding claim 11, the probe carrier of claim 1 is discussed above in Sections 8 and 12.

While Alfenito teaches the number of dots per array is different and that one to 25 dots are present (Example 8), Alfenito does not specifically teach the maximum number of spots in the arrays differs 100 to 1000 times.

However, Ares et al teach arrays comprising a plurality of different oligonucleotide spot patterns, wherein each spot pattern is to a different target nucleic acid (paragraph 0072), and that the number of spots of a typical array is about twenty or about twenty thousand (paragraph 0071), which has the added advantage of being useful in high throughput applications (paragraph 0072). Thus, Ares et al teach the known technique of providing spot densities having 1000-fold differences.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier having different numbers of probe spots in each area as taught by Alfenito so that range of the number of spots is such that the first area has 20 probes and another area has 20,000 probes as taught by Ares et al to arrive at the instantly claimed carrier with a reasonable

expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of being useful in high throughput applications as explicitly taught by Ares et al (paragraph 0072). In addition, it would have been obvious to the ordinary artisan that the known technique of having spot arrays having ranges of spot numbers of 1000 times difference of Ares et al could have been applied to the carrier of Alfenito with predictable results because the known technique of having spot arrays having ranges of spot numbers of 1000 times difference of Ares et predictably results in a reliable array configuration for detecting target molecules.

15. Claims 1 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiment of dependent claim 11.

Regarding claim 11, Kronick et al teach the probe carrier of claim 1 comprising a carrier in the form of a solid support (Abstract and Figure 6) having thereon a plurality of probe spots (i.e., features; paragraph 0063). The array comprises different regions, wherein each region comprises multiple features (paragraph 0014), and each feature is a spot (paragraph 0030). The addresses of each spot, feature, and region are known because the array is fabricated (paragraph 0030). Kronick et al teach different probes that capable of specifically binding to a target substance (paragraph 0090), and the

probes bind to genes (paragraph 0166). Kronick et al also teach the relative total feature areas (i.e., regions) have different numbers of features of the same size and that the population or probes therein are dependent upon the suspected relative abundance of the targets (paragraph 0090); thus, the carrier comprises two different areas (regions) comprising features (spots) to different genes, and the number of spots in each region is different because the number of spots depends on the expected abundance of the target detected in each area.

While Kronick et al do not specifically teach the maximum number of spots in the arrays in the 12g-12m area differs 100 to 1000 times between the minimum number of spots of the arrays in the 12n-12t area of Figure 6, Kronick et al do teach each array has a different number of spots (i.e., feature number; paragraph 0090). Kronick et al also teach the number of spots of a typical array is about ten or about ten thousand (paragraph 0116). The embodiment of Figure 6 has each of the arrays 12g-12m having the same number of spots, and each of the arrays 12n-12t having the same number of spots as described above. Thus, in the embodiment wherein array 12g has 10 spots and array 12n has 10,000 spots (paragraph 0016), arrays 12g-12m collectively have 70 spots total (i.e., 7 arrays of 10 spots), and arrays 12n-12t collectively have 70,000 spots total (i.e., 7 arrays of 10,000 spots), and the ratio is 1000 between the minimum number of spots (i.e., arrays 12g-12m) and the maximum number of spots (i.e., arrays 12n-12t).

16. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003) in view of Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002) as applied to claim 1 above.

Regarding claim 11, the probe carrier of claim 1 is discussed above in Section 11.

While Ares et al do not explicitly teach the first pattern has 1000 times the number of spots as the second pattern, Ares et al do teach the number of spots of a typical array is about twenty or about twenty thousand (paragraph 0071), which has the added advantage of being useful in high throughput applications (paragraph 0072). Thus, Ares et al teach the known technique of providing spot densities having 1000-fold differences.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier having different numbers of probe spots in each area as taught by Ares et al (alternatively in view of Alfenito) so that range of the number of spots is such that the first area has 20 probes and another area has 20,000 probes as taught by Ares et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of being useful in high throughput

applications as explicitly taught by Ares et al (paragraph 0072). In addition, it would have been obvious to the ordinary artisan that the known technique of having spot arrays having ranges of spot numbers of 1000 times difference of Ares et al could have been applied to the carrier of Ares et al (alternatively in view of Alfenito) with predictable results because the known technique of having spot arrays having ranges of spot numbers of 1000 times difference of Ares et al predictably results in a reliable array configuration for detecting target molecules.

17. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002) as applied to claim 1 above, and further in view of Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003).

Regarding claim 23, the carrier of claim 1 is discussed above in Sections 8 and 12.

Alfenito does not teach the amount of immobilized spot is known.

However, Ares et al teach the amount of probes per immobilized spot is known; namely, 1 ng of probes are present in the spots, which has the added advantage of guaranteeing that the amount present is the spots is sufficient for adequate hybridization and detection of the target (paragraph 0075). Thus, Ares et al teach the known technique of providing a known amount of probe in a spot.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier of Alfenito so that

amount of probe in each spot is known as taught by Ares et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of guaranteeing that the amount present is the spots is sufficient for adequate hybridization and detection of the target as explicitly taught by Ares et al (paragraph 0075). In addition, it would have been obvious to the ordinary artisan that the known technique of providing a known amount of probe in a spot of Ares et al could have been applied to the carrier of Alfenito with predictable results because the known technique of providing a known amount of probe in a spot of Ares et al predictably results in a reliable amount of probe for subsequent assay.

18. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over of Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002) in view of Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003) as applied to claim 1 above, and further in view of Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004).

Regarding claim 25, the carrier of claim 23 is discussed above in Section 17.

While Alfenito teaches the carrier comprises spots having complementary probes for measuring gene expression (column 2, lines 55-67) and human genes (Example 20), and while Ares et al teach the complementary probes in the spots are for gene expression (paragraph 0062) and that the spots correspond to human genes (paragraph

0076), neither Alfenito nor Ares et al explicitly teach the number of spots in each area is proportional to an average amount of expression of the gene.

However, Kronick et al teach a carrier having different regions, wherein each region comprises multiple features (paragraph 0014), and each feature is a spot (paragraph 0030). The addresses of each spot, feature, and region are known because the array is fabricated (paragraph 0030). Kronick et al teach different probes that capable of specifically binding to a target substance (paragraph 0090), and the probes bind to genes (paragraph 0166). Kronick et al also teach the relative total feature areas (i.e., regions) have different numbers of features of the same size and that the population or probes therein are dependent upon the suspected relative abundance of the targets (paragraph 0090), wherein the number of probes is proportional to the square root of the expected (i.e., average) signal for each target (paragraph 0097). Kronick et al also teach the probe densities have the added advantage of allowing customized arrays to be made for a target (paragraph 0076). Thus, Kronick et al teach the known technique of providing amounts of probe molecules so that number of spots is proportional to an average (i.e., expected) amount of target gene is a sample.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier comprising probe spots for measuring gene expression in a human as taught by Alfenito so that number of spots is proportional to the expected average amount of a target as taught by Kronick et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said

modification would have resulted in a carrier having the added advantage of allowing customized arrays to be made for a target as explicitly taught by Kronick et al (paragraph 0076). In addition, it would have been obvious to the ordinary artisan that the known technique of providing amounts of probe molecules so that number of spots is proportional to the average amount in the sample as taught by Kronick et al could have been applied to the carrier of Alfenito with predictable results because the known technique of providing amounts of probe molecules so that number of spots is proportional to the average amount in the sample as taught by Kronick et al predictably results in an array configuration useful in detecting genes.

19. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004, filed 25 November 2003) as applied to claim 23 above, and further in view of Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002).

Regarding claim 25, the carrier of claim 23 is discussed above in Section 9.

While Kronick et al the number of probes (and thus, the number of spots) is proportional to the square root of the expected (i.e., average) signal for each target (paragraph 0097), and that the spots are for gene expression (paragraph 0002), Kronick does not teach the probes are for human genes.

However, Alfenito teaches a carrier that comprises spots having complementary probes for measuring gene expression (column 2, lines 55-67) and human genes (Example 20). Alfenito also teaches the carrier has the added advantage of allowing

localization of genes involved in polygenic diseases (Example 21). Thus, Alfenito teaches the known technique of having spots for measuring human gene expression.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier of Kronick et al so that the spots are to human gene expression as taught by Alfenito to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing localization of genes involved in polygenic diseases as explicitly taught by Alfenito (Example 21). In addition, it would have been obvious to the ordinary artisan that the known technique of providing of spots for human gene expression as taught by Alfenito could have been applied to the carrier of Kronick et with predictable results because the known technique of providing of spots for human gene expression as taught by Alfenito predictably results in an carrier useful for studying human genetic diseases.

20. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004, filed 25 November 2003) as applied to claim 23 above, and further in view of Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003

It is noted that while claim 25 is rejected under 35 U.S.C. 103(a) as described above in Section 19, the claim is also obvious using the interpretation outlined below.

Regarding claim 25, the carrier of claim 23 is discussed above in Section 9.

While Kronick et al the number of probes (and thus, the number of spots) is proportional to the square root of the expected (i.e., average) signal for each target (paragraph 0097), and that the spots are for gene expression (paragraph 0002), Kronick does not teach the probes are for human genes.

However, Ares et al teaches a carrier that comprises spots for gene expression (paragraph 0062) and that the spots correspond to human genes, which has the added advantage of allowing detection of genes implicated in cancer (paragraph 0076). Thus, Ares et al teach the known technique of having spots for measuring human gene expression.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier of Kronick et al so that the spots are to human gene expression as taught by Ares et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing detection of genes implicated in cancer as explicitly taught by Ares et al (paragraph 0076). In addition, it would have been obvious to the ordinary artisan that the known technique of providing of spots for human gene expression as taught by Ares et al could have been applied to the carrier of Kronick et with predictable results because the known technique of providing of spots for human gene expression as taught by Ares et al predictably results in an carrier useful for studying human genetic diseases.

21. Claim 25 is rejected under 35 U.S.C. 103(a) as obvious over Ares et al (U.S. Patent Application Publication No. US 2004/0009512 A1, published 15 January 2004, filed 25 April 2003) alternatively in view of Alfenito (U.S. Patent No. 6,355,419 B1, issued 12 March 2002) as applied to claim 23 above, and further in view of Kronick et al (U.S. Patent Application Publication No. US 2004/0115722 A1, published 17 June 2004).

Regarding claim 25, the carrier of claim 23 is discussed above in Section 11.

While Ares et al teach the complementary probes in the spots are for gene expression (paragraph 0062) and that the spots correspond to human genes (paragraph 0076), and while Alfenito teaches the carrier comprises spots having complementary probes for measuring gene expression (column 2, lines 55-67) and human genes (Example 20), neither Ares et al nor Alfenito explicitly teach the number of spots in each area is proportional to an average amount of expression of the gene.

However, Kronick et al teach a carrier having different regions, wherein each region comprises multiple features (paragraph 0014), and each feature is a spot (paragraph 0030). The addresses of each spot, feature, and region are known because the array is fabricated (paragraph 0030). Kronick et al teach different probes that capable of specifically binding to a target substance (paragraph 0090), and the probes bind to genes (paragraph 0166). Kronick et al also teach the relative total feature areas (i.e., regions) have different numbers of features of the same size and that the population or probes therein are dependent upon the suspected relative abundance of the targets (paragraph 0090), wherein the number of probes is proportional to the

square root of the expected (i.e., average) signal for each target (paragraph 0097). Kronick et al also teach the probe densities have the added advantage of allowing customized arrays to be made for a target (paragraph 0076). Thus, Kronick et al teach the known technique of providing amounts of probe molecules so that number of spots is proportional to an average (i.e., expected) amount of target gene is a sample.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier comprising probe spots for measuring gene expression in a human as taught by Ares et al (alternatively in view of Alfenito) so that number of spots is proportional to the expected average amount of a target as taught by Kronick et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing customized arrays to be made for a target as explicitly taught by Kronick et al (paragraph 0076). In addition, it would have been obvious to the ordinary artisan that the known technique of providing amounts of probe molecules so that number of spots is proportional to the average amount in the sample as taught by Kronick et al could have been applied to the carrier of Ares et al (alternatively in view of Alfenito) with predictable results because the known technique of providing amounts of probe molecules so that number of spots is proportional to the average amount in the sample as taught by Kronick et al predictably results in an array configuration useful in detecting genes.

Response to Arguments

22. Applicant's arguments filed 22 June 2009 (hereafter the "Remarks") have been fully considered but they are not persuasive for the reasons discussed below.

A. Applicant argues on page 5 of the Remarks that Kronick et al do not teach the number of spots differed depending on the genes.

However, as detailed in the rejections above, Kronick et al teach a carrier comprising different probes that are capable of specifically binding to a target substance (paragraph 0090), and the probes bind to genes (paragraph 0166). Kronick et al also teach the relative total feature areas (i.e., regions) have different numbers of features of the same size and that the population or probes therein are dependent upon the suspected relative abundance of the targets (paragraph 0090); thus, the carrier comprises two different areas (regions) comprising features (spots) to different genes, and the number of spots in each region is different because the number of spots depends on the expected abundance of the target detected in each area.

B. Applicant argues on pages 5-6 of the Remarks that Kronick et al does not disclose of suggest the benefits provided by the features of the claimed invention.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a more stable probe forming process, high precision) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Further, the courts have held that "while features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function." *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). In addition, "[A]pparatus claims cover what a device *is*, not what a device *does*." *Hewlett-Packard Co. v. Bausch &Lomb Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990) (emphasis in original). Therefore, the various processes recited in Applicant's arguments (e.g., more stable probe forming, high precision) fail to define additional structural elements of the claimed carrier. Because the cited prior art teaches the structural elements of the claims, the claims are anticipated by, and obvious over, the prior art cited above. See MPEP § 2114.

Conclusion

23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Robert T. Crow
Examiner
Art Unit 1634

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